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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/032,257
Filing Date: December 21, 2001
Appellant(s): KRULEVITCH ET AL.

Eddie E. Scott
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 18, 2006 appealing from the Office action mailed March 6, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 5,985,217	Krulevitch et al.	11-1999
US 6,219,474	Krulevitch et al.	11-2001
WO 99/33559	Pourahmadi et al.	07-1999

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-5 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krulevitch et al.(US 5,985,217 or US 6,319,474) in view of Pourahmadi et al.(WO 99/33559).

The references of Krulevitch et al. disclose a microfabricated biopsy and analysis instrument (30) that includes a body (See Figure 3C) including a silicon substrate (31) and a glass substrate (32) positioned together. The device includes a cutter with a sharp edge (35) and a tapered opening (34). A specimen chamber is defined by the volume between the tapered opening (34) and microchannel (40). This chamber is located in the silicon substrate and glass substrate immediately below the cutter (See Figure 3C). The device includes a specimen treatment and analysis chamber (40) located in the silicon substrate and glass substrate abutting and connected directly to the specimen chamber and located adjacent the specimen chamber. The device includes an analysis unit (47) in the specimen treatment and analysis chamber (40).

While the references of Krulevitch et al. disclose that the specimen treatment and analysis chamber (40) is communicated with chamber (46) and discloses that the specimen within chamber (40) can be treated with a chemical (See column 5, lines 20-47, of '217, and column 5, lines 22-49, of '474), the instant claims differ by reciting that the body of the device includes a PCR chamber with a heating unit directly connected to the specimen treatment and analysis chamber.

The reference of Pourahmadi et al. discloses that it is known in the art to combine a microfabricated sample preparation device, including tissue slicing or cutting, with a microfabricated analyte detection structure and/or a microfabricated polynucleotide amplification structure. The reference of Pourahmadi et al. discloses a microfabricated biopsy and genetic analysis instrument that includes a cutter section and specimen chamber (103) located below the cutter section. See page 20, line 27, to page 21, line 10, which discloses that the opening of the specimen chamber (sample port, 103) can include a mesh that slices a tissue specimen. The instrument includes a specimen treatment section (including treatment chambers 107, 119, 122, 141) located adjacent the specimen chamber (103) and a PCR reaction chamber section that is integral or abuts the specimen treatment section. See page 12, lines 13-26, which discloses that the PCR reaction chamber (143) can be integral or separable relative to the sample treatment section of the instrument. Note the reference of Pourahmadi et al. discloses that the heating unit for performing PCR can be located within or adjacent the channel or chamber (See page 37, lines 19-28).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the references of Krulevitch et al. with

a PCR chamber directly connected to the sample treatment chamber for the known and expected result of further processing the tissue sample within the same device as suggested by the reference of Pourahmadi et al. while providing the advantages associated with the structure of the device of Krulevitch. Note the references of Krulevitch et al. disclose that the disclosed device can be incorporated into a system microfluidic system using existing microvalves and pumps (See column 5, lines 49-59, of '217, and column 5, lines 50-60, of '474) and that the device is intended to be used for acquiring specimens for DNA analysis (See column 1, lines 62-65, of '217, and column 1, lines 65-67, of '474).

With respect to the use of the "consisting of" language, the presence of purification sections and other sample processing zones and/or structures, as disclosed by the reference of Pourahmadi et al., is considered to fall within the claimed "specimen treatment and analysis chamber" because the instant specification and/or Appellants' concise explanation of the claimed subject matter indicate that the claimed "specimen treatment and analysis chamber" includes additional structural elements that are not positively recited in the instant claims. For example, page 5, lines 3-5, of the instant specification states "Other features include sorting of cells so that the PCR could be performed on very specific cell from the overall sample, or filtering to select specific cells". Page 5, lines 14-16, of the instant specification state "While only one inlet channel is shown, additional inlet channels can be utilized for introducing cell lysing solution, or other sample treatment solutions, to lyse or otherwise treat the biopsied tissue". Page 6, lines 23-26, of the instant specification and page 6 of the Appeal Brief filed 7/18/2006 states "The specimen treatment microchannel 21 includes any desired number of channels 30 formed in the glass substrate 24, only one being shown, and which contains a chemical solution 31 for

treatment of the tissue specimen or sample 29". In view of these disclosures, the presence of additional structural elements, i.e. filters, reagent channels, reagent reservoirs, etc., are not considered to be precluded by the use of the transitional claim language "consisting of" linked with claim language "specimen treatment and analysis chamber".

Alternatively, provision of a device that is devoid of reagents and/or controllers, would have been obvious when providing a disposable device wherein the control devices can be reused with other devices. Also, based merely on the source of the sample to be detected and/or the reagents employed, whether or not the system includes a DNA purification zone would have been well within the purview of one having ordinary skill in the art.

With respect to claim 2, the references of Krulevitch et al. disclose that the cutting edge (35) has a smooth edge with atomic sharpness capable of cutting very thin specimens of tissue (See column 6, lines 28-38, of '217, and column 6, lines 28-39, of '474).

With respect to claim 3, the references of Krulevitch et al. disclose that the cutter is constructed of silicon (See column 5, lines 1-20, of '217, and column 5, lines 1-20, of '474).

With respect to claims 4 and 5, the references of Krulevitch et al. disclose that analysis unit (47) is an optical analysis unit (See column 5, lines 29-31, of '217 and column 5, lines 30-32, of '474) and construction of the microchannel device of silicon and glass substrates (See column 3, lines 1-12, of '217 and column 3, lines 1-13, of '474). The reference of Pourahmadi et al. discloses the use of microchannels (See Figure 2) to connect the sample chamber (103) with the PCR reaction chamber (143). Also the reference discloses the use of planar members, including glass, to form the device (See page 26, line 35, to page 27, line 28).

With respect to claim 16, the specimen treatment and analysis chamber (40) includes a chemical solution channel (40), an optical window (32) and optical detection system (47).

With respect to claim 17, the structures of the modified primary reference as suggested above would all be formed in the same body.

With respect to claim 18, the reference of Krulevitch et al. discloses that the cutting edge (35) has a smooth edge with atomic sharpness capable of cutting very thin specimens of tissue.

With respect to claim 19, the reference of Krulevitch et al. discloses the location of the optical analysis window and detection device with respect to specimen and analysis chamber (40) which is in communication with the specimen chamber.

(10) Response to Argument

With respect to the rejection of Claims 1-5 and 16-19 under 35 U.S.C. 103(a) as being unpatentable over Krulevitch et al.(US 5,985,217 or US 6,319,474) in view of Pourahmadi et al.(WO 99/33559), Appellants argue that the rejection is improper for the following reasons:

Argument 1 (See pages 8-10 of the Appeal Brief filed 7/18/2006): The primary references of Krulevitch et al. fail to disclose the instantly claimed elements (1) "PCR chamber" and (2) "a heating unit". Since the reference does not disclose elements (1) and (2), the reference cannot discloses element (3) "a PCR reaction chamber in said silicon substrate and said glass substrate directly abutting and connected directly to said specimen treatment and analysis chamber" and element (4) "a heating unit in said body adjacent said PCR reaction chamber". Finally, Appellants stress that the references of Krulevitch et al. fail to disclose element (5) "a

microfabricated biopsy and analysis instrument for biopsy and analysis of tissue with minimal handling of the tissue, "consisting of:" the specific combinations of elements enumerated in Appellants' claims 1-5 and 16-19 on appeal".

In response to argument 1 above, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the Examiner has relied upon the combination of the teachings of the references of Krulevitch et al. and Pourahmadi et al. to address the instant claim limitations. Specifically, the references of Krulevitch et al. disclose that the disclosed device can be incorporated into a system microfluidic system using existing microvalves and pumps (See column 5, lines 49-59, of '217, and column 5, lines 50-60, of '474) and that the device is intended to be used for acquiring specimens for DNA analysis (See column 1, lines 62-65, of '217, and column 1, lines 65-67, of '474) while the reference of Pourahmadi et al. discloses that it is known in the art to combine a microfabricated sample preparation device, including tissue slicing or cutting, with a microfabricated analyte detection structure and/or a microfabricated polynucleotide amplification structure. As a result, the Examiner is of the position that the combination of the references as set forth in the rejection of claims 1-5 and 16-19 under 35 USC 103 is proper and meets every claim limitation set forth in the claims.

Argument 2 (See pages 10-13 of the Appeal Brief filed 7/18/2006): The instant claims employ the "consisting of" preamble which requires a specific combination of elements not found or suggested in the references of Krulevitch et al. or in the reference of Pourahmadi et al.

Appellants stress that the reference of Pourahmadi et al. shows a complex device that includes numerous elements in an entirely different combination that that required of the instant invention "consisting of" the specific combination of elements. Specifically, Appellants argue that the reference of Pourahmadi et al. requires and/or includes many intermediate elements between the sample port (103) and the reaction chamber (143) that would be precluded by the "consisting of" language of the instant claims.

In response to argument 2 above, the presence of "intermediate elements" between the sample port and reaction chamber, as disclosed by the reference of Pourahmadi et al., is considered to fall within the claimed "specimen treatment and analysis chamber" because the instant specification and/or Appellants' concise explanation of the claimed subject matter indicate that the claimed "specimen treatment and analysis chamber" includes additional structural elements that are not positively recited in the instant claims. For example, page 5, lines 3-5, of the instant specification states "Other features include sorting of cells so that the PCR could be performed on very specific cell from the overall sample, or filtering to select specific cells". Page 5, lines 14-16, of the instant specification state "While only one inlet channel is shown, additional inlet channels can be utilized for introducing cell lysing solution, or other sample treatment solutions, to lyse or otherwise treat the biopsied tissue". Page 6, lines 23-26, of the instant specification and page 6 of the Appeal Brief filed 7/18/2006 states "The specimen treatment microchannel 21 includes any desired number of channels 30 formed in the glass substrate 24, only one being shown, and which contains a chemical solution 31 for treatment of the tissue specimen or sample 29". In view of these disclosures, the presence of additional structural elements, i.e. filters, reagent channels, reagent reservoirs, etc., are not

considered to be precluded by the use of the transitional claim language "consisting of" linked with claim language "specimen treatment and analysis chamber". Alternatively, provision of a device that is devoid of reagents and/or controllers, would have been obvious when providing a disposable device wherein the control devices can be reused with other devices. Also, based merely on the source of the sample to be detected and/or the reagents employed, whether or not the system includes a DNA purification zone would have been well within the purview of one having ordinary skill in the art.

Argument 3 (See pages 10-14 of the Appeal Brief filed 7/18/2006): The references of Krulevitch et al. and Pourahmadi et al. lack suggestion or motivation to modify or combine the reference teachings. To support their position, Appellants stress that the references of Krulevitch et al. fail to disclose the claimed "PCR reaction chamber" and/or "a heating unit" and/or an apparatus "consisting of" the combination of elements required of the instant claims. Appellants also stress that the reference of Pourahmadi et al. involves a different combination of elements than that required of the instant claims and the reference fails to show "a microfabricated biopsy and analysis instrument for biopsy and analysis of tissue with minimal handling of the tissue, "consisting of:" the specific combinations of elements enumerated in Appellants' claims 1-5 and 16-19 on appeal"; "a PCR reaction chamber in said silicon substrate and said glass substrate directly abutting and connected directly to said specimen treatment and analysis chamber"; and "a heating unit in said body adjacent said PCR reaction chamber"; wherein said specimen treatment and analysis chamber and said PCR reaction chamber are located in said silicon substrate and said glass substrate and said cutter is constructed of silicon and wherein said glass

substrate is bonded to said silicon substrate"; and/or wherein said optical detection system is located to provide optical analysis of the tissue through said optical window of said specimen treatment and analysis chamber".

In response to argument 3 above, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the Examiner has relied upon the combination of the teachings of the references of Krulevitch et al. and Pourahmadi et al. to address the instant claim limitations. Additionally, the Examiner maintains that the combination of the references as recited in the 35 USC 103 rejection of record meets the structure of the claimed device for the reasons specifically set forth in the rejection of record. Note the reference of Krulevitch et al. discloses a majority of the structural elements absence a PCR chamber and heater. The reference of Pourahmadi et al. discloses that it is known in the art to combine a tissue-cutting device with a PCR device. Furthermore, the reference of Krulevitch et al. discloses that the tissue samples obtained by the device can be used for DNA analysis (See column 1, lines 62-65) and that the device can be incorporated into a microfluidic system (See column 5, lines 49-59). The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Examiner is of the opinion that since the reference of Krulevitch et al.

discloses a cutting device which can be used for DNA analysis and can be incorporated into a microfluidic and the reference of Pourahmadi et al. discloses that a tissue cutting or sampling device can be combined with a PCR device, one of ordinary skill in the art would have readily recognized the advantages of using the cutting device disclosed by the reference of Krulevitch et al. to provide a sample to a PCR analysis device. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). As a result, the Examiner is of the position that the combination of the references as set forth in the rejection of claims 1-5 and 16-19 under 35 USC 103 is proper and meets every claim limitation set forth in the claims.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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